WO 2004/055514 PCT/EP2003/051028

57

What is claimed is:

- A method for diagnosis of carcinomas and their precursor lesions and/or prognosis of disease course comprising
 - a) obtaining a sample from an individual
 - b) determining the levels of one or more DNase molecules;
 - c) comparing the levels of said DNase molecules within said sample to the contents within a corresponding control sample, not affected by the disease being tested;
 - d) wherein the diagnosis or prognosis of disease course is predicted from considering a significant change relative to the wild type level of at least one single DNase molecule or of a set of DNase molecules as indicative of said disorder or of the prognosis of the disease course.
- 2. The method according to Claim 1, wherein the DNase is selected from a group comprising
 - a) DNase I-like 1 (DNase X) (NM_006730);
 - b) DNase I-like 3 (also called DNase gamma) (AF047354):
 - c) DNase I (AJ298844);
 - d) DNase II (AB004574);
 - e) DNase I-like 2 (AK098028);
 - f) caspase activated DNase (AB013918);
 - g) DNase KIAA0218 (D86972);
 - h) DNase II-like DNase (AF274571); and
 - i) DFF-45 (AF087573).
- 3. The method according to Claim 1 or 2, wherein the detection of the DNase molecules comprises the detection of the accessibility of particular regions of the DNase molecules.
- 4. The method according to Claims 1 3, wherein the subcellular localization of the DNase is determined.
- 5.The method of any of the preceding Claims, wherein the sample is selected from a group comprising a liquid containing nucleic acids, polypeptides or fragments thereof, a liquid containing cells or cell debris, a body fluid, a tissue sample and a cell sample.
- 6. The method of Claim 5, wherein the sample is blood, plasma, serum, liquor, lymph, bone marrow, swabs, washes, lavages, secretions, transsudates, exsudates, sputum, stool, urine, semen, cell- and tissue-samples, punctuates or biopsies.
- 7. The method according to any one of the preceding Claims, wherein the carcinoma is selected from a group comprising cancer of the head and the neck, cancer of the respiratory tract, cancer of

the gastrointestinal tract, cancer of the skin and its appendages, cancer of the central and peripheral nervous system, cancer of the urinary system, cancer of the reproductive system, cancer of the endocrine system, cancer of the soft tissues and bone, cancer of the lymphopoietic and hematopoietic system, breast cancer, lung cancer, cervical cancer, colorectal cancer or anogenital cancer.

- 8. A method according to any one of the Claims 1 7, wherein the detection of the expression of the DNase molecule is carried out by detection of DNase enzyme activity in samples.
- 9.A method according to any one of the Claims 1 7, wherein the detection of the expression of the DNase molecule is carried out using at least one probe specifically binding to the marker molecules to be detected.
- 10. A method according to Claim 9, wherein the probe is detectably labelled.
- 11. The method according to Claim 10, wherein the label is selected from the group consisting of a radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, a biologically relevant binding structure such as biotin or digoxygenin or an enzyme.
- 12. The method according to Claims 9 11, wherein at least one probe is an antibody, a fragment of an antibody, a peptidomimetic comprising an antigen binding epitope or a mini-antibody.
- 13. The method according to Claim 12, wherein the detection comprises an immuno-cytochemical detection procedure.
- 14. The method according to Claims 9 11, wherein at least one probe being a nucleic acid hybridising to a marker nucleic acid is used for the detection of the DNase marker molecules.
- 15. The method according to Claim 14, wherein the detection reaction comprises a nucleic acid amplification reaction.
- 16. The method according to Claims 14 15, which is used for in situ detection.
- 17. A method according to any one of the preceding Claims, which is used in the course of an *in vivo* or *in vitro* molecular imaging method.
- 18. A method according to any one of the preceding Claims, which is carried out in the course of early diagnosis of disorders, of minimal residual disease diagnosis or of screening tests.
- 19. A test-kit for carrying out the method according to any one of the preceding Claims, comprising at least

- a) reagents for the detection of DNase nucleic acids and/or DNase polypeptides;
- b) the reagents and buffers commonly used for carrying out the detection reaction, such as buffers, detection-markers, carrier substances and others,

which is a research kit, a diagnostic kit or a point of care test kit.

- 20. A test-kit according to Claim 19, wherein the reagent for detection of the DNase nucleic acids and/or DNase polypeptides is an agent specifically binding to said nucleic acids and/or polypeptides.
- 21. A method of identifying and obtaining a drug candidate for therapy carcinomas and their precursor lesions comprising the steps of
 - a) contacting a DNase polypeptide or a cell expressing said polypeptide in the presence of components capable of providing a detectable signal in response to DNase activity, cell proliferation or cell differentiation with said drug candidate to be screened under conditions to allow DNase activity, cell proliferation or changes in cell differentiation and
 - b) detecting presence or absence of a signal or increase of the signal generated from DNase activity, cell proliferation or cell differentiation, wherein the presence or increase of the signal is indicative for a putative drug.
- 22. A compound selected from a group comprising
 - a) a binding partner to a DNase polypeptide:
 - b) an activators/agonists or inhibitors/antagonists of a DNase polypeptide;
 - c) an activator or inhibitor of the expression of a DNase polypeptide; and
 - d) a drug candidate identifiable by a method according to Claim 21;

for use in the detection and treatment of carcinomas and their precursor lesions.

- 23.Use of a compound selected from a group comprising
 - a) one or more DNase molecules being nucleic acids or polypeptides;
 - b) one or more activators/agonists or inhibitors/antagonists of a DNase polypeptide;
 - c) one or more activators or inhibitors of the expression of a DNase polypeptide;
 - d) one or more binding partners of DNase polypeptides; and
 - e) one or more drug candidates identifiable by a method according to Claim 21;

for production of a medicament useful for treating carcinomas and their precursor lesions.

- 24. The use according to Claim 23, wherein the carcinoma is selected from a group comprising cancer of the head and the neck, cancer of the respiratory tract, cancer of the gastrointestinal tract, cancer of the skin and its appendages, cancer of the central and peripheral nervous system, cancer of the urinary system, cancer of the reproductive system, cancer of the endocrine system, cancer of the soft tissues and bone, cancer of the lymphopoietic and hematopoietic system, breast cancer, anogenital cancer or colorectal cancer.
- 25. A pharmaceutical composition comprising at least one compound selected from a group consisting of
 - a) one or more DNase molecules being nucleic acids or polypeptides;
 - b) one or more activators/agonists or inhibitors/antagonists of a DNase polypeptide;
 - c) one or more activators or inhibitors of the expression of a DNase polypeptide;
 - d) one or more binding partners of DNase polypeptides;
 - e) or one or more drug candidates identifiable by a method according to Claim 21;

for treating carcinomas and their precursor lesions.

26. A method for treatment of carcinomas and their precursor lesions comprising administering to an individual a compound according to Claim 22 or a pharmaceutical composition according to Claim 25.